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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/361,576	07/27/1999	BRENT R. STOCKWELL	2001180-0028	5706

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/361,576	STOCKWELL ET AL.	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *57-60,63,64,66-69,71-81 and 83-107* is/are pending in the application.

4a) Of the above claim(s) *58,84 and 105-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57,59,60,63,64,66-69,71-81,83 and 85-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 July 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S. 020

DETAILED ACTION

Application and Claims Status

1. Applicant's amendment and response filed 02/24/2005 is acknowledged and entered. Claims 65, and 70 have been canceled. Claims 57, 58, 64, 66, 67, and 69 have been amended. Claims 105-107 have been added.

2. Claims 61-62 have been canceled; and Claims 57-59, 63-65, and 81 have been amended by the amendment filed on 05/10/2004.

3. Claim 82 was canceled; Claims 57-81 and 83-103 were amended; and Claim 104 was added by the amendment filed on 05/21/2003.

4. Claims 1-56 were cancelled and Claims 57-103 were added by the amendment filed on 06/05/2002.

5. Claims 57-60, 63, 64, 66-69, 71-81, and 83-107 are pending.

Election/Restrictions

6. The currently amended claim 58 and the newly submitted claims 105-107 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Group A (Claims 57, and 59-104) is drawn to a high-throughput method for screening one or more test compounds.

Group B (Claims 58-107) is drawn to a high-throughput method for obtaining a functional fingerprint of one or more test compounds.

The inventions of Group A and Group B are drawn to two different methods, which differ in their method steps, i.e. requiring different reagents and/or producing different products/results. The different method steps have different functions and modes of operation. Group A requires the step of assaying for association between the antibody and the biological component in the reaction vessels to assess the presence or amount of the biological component, thereby revealing the effect of the test compound on the biological or chemical process. Group B requires the step of recording the effects of each test compound on the plurality of intracellular biological or chemical processes, thereby establishing a functional fingerprint for each test compound. Thus these different inventions as claimed have different method steps that have different functions and modes of operation (MPEP § 806.04, MPEP § 808.01).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 58, and 105-107 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

7. Applicant has elected the following species for the elected invention (Claims 57, 59-104) in the reply filed on 10/15/02:

a. A species of ligand. Applicant elected antibody.

b. A species of second ligand. Applicant elected antibody.

c. A species of reagent. Applicant elected 5-bromodeoxyuridine.

d. A species of number of different cell line use. Applicant elected one.

8. Claim 84 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/15/02.

9. Claims 57, and 59-104 are treated on the merit in this Office Action.

Maintained Rejection(s)

Claim Rejections - 35 USC § 103

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 57, 59-60, 63-71, 76-81, 83, and 85-104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stylli et al. (US Patent 5,985,214) and Photiou et al. (*European Journal of Cancer*, **3/1997**, 33(3), pgs. 463-470).

The instant claim 57 recites a high-throughput method for screening one or more test compounds to identify those that exert an effect on an intracellular biological or chemical process. The method comprises the steps of 1) introducing into each of a plurality of reaction vessels: a plurality of cells, and one or more test compounds whose effect on an intracellular biological or chemical process is to be evaluated; 2) introducing into each of the reaction vessels an antibody characterized in that it associates intracellularly with a biological component whose presence or amount reveals the effect of a given test compound on the biological or chemical process; and 3) assaying for association between the antibody and the

component in the reaction vessels. The plurality of reaction vessels comprises at least 96 reaction vessels.

Stylli et al. teaches an automated method and system for identifying chemicals having useful activity such as biological activities of chemicals and collecting informations resulting from such a process (e.g. see Abstract; col. 2, lines 35-41; col. 6, lines 1-24). The method comprise of testing a therapeutic chemical for modulating activity of a target in a cell-based assay (e.g. see col. 38, lines 46-67; col. 39, lines 1-9; col. 43, lines 6-9). The method comprises dispensing the reagents (compounds) into the addressable sample wells, which contains a predetermined volume of the sample (test cells) (e.g. see col. 6, lines 25-40; col. 8, lines 14-18). Additionally, Stylli et al. disclose the method of dispensing live cell cultures into the sample wells (e.g. see col. 59, lines 20-32). The wells include formats such as 96 wells, 384 wells, or greater (e.g. see col. 15, lines 14-22). Stylli et al. disclose that various different cell-based assay can be employed with its systems wherein the assays include intracellular receptors (e.g. see col. 38, lines 46-47; col. 39, line 60 to col. 40, line 50; col. 42, line 10-15) and also various method of detection of the compound interaction with the target includes fluorescent measurement (e.g. see col. 27, lines 29-35; col. 28, lines 15-17; col. 39, lines 1-67 thru col. 42, lines 1-23). The compounds tested include combinatorial compounds (e.g. see col. 43, lines 21-44).

Furthermore, the features of remaining dependent claims, i.e. volume of the wells or wells format of claims 91-101 are either specifically described by the reference, or constitute obvious variations in parameters which are routinely modified in the art, and which have not been described as critical to the practice of the invention.

The cell-bases assay of Stylli et al. does not expressly include in the cell-base assay wherein the steps are introducing into the reaction vessels an antibody that is associated with a biological component and introducing a secondary ligand that binds specifically to the antibody.

Photiou et al. disclose a method for evaluating the in vitro antiproliferative activity (inhibiting cell replication and therefore DNA synthesis) of drugs as single agents and as combinations using human melanoma cell lines G361 and StMl11a (Abstract). Photiou et al. disclose an indirect immunofluorescence method in which cells are seeded on glass cover slips placed in 24-well plates, treated with drug(s), fixed, permeated, incubated with rabbit anti-tubulin antibodies, washed, and incubated with goat anti-rabbit antibody conjugated to FITC (secondary ligand) (e.g. see pg. 465, column 1). Photiou et al. discloses the interpretation of the tubulin immunofluorescence data, including the intracellular localization of the primary and secondary antibodies (e.g. pg. 466, columns 1 and 2). The prevention of tubulin polymerization is a "post-translational event" and an "intracellular biochemical reaction."

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include in the cell-base assay wherein the steps are introducing into the reaction vessels an antibody that is associated with a biological component and introducing a secondary ligand that binds specifically to the antibody as taught by Photiou et al. in the method of Stylli et al. One of ordinary skill in the art would have been motivated to include in the cell-base assay wherein the steps are introducing into the reaction vessels an antibody that is associated with a biological component and introducing a secondary ligand that binds specifically to the antibody in the method of Stylli et al. since Stylli et al. disclose that any type of cell-base assay can be employed with system of Stylli et al. (e.g. see col. 38, lines 46-47; col.

39, line 60 to col. 40, line 50; col. 42, line 10-15). Thus any type of cell-base assay methodologies can be use in the system of Stylli et al. and the type of cell-base assay use would be a choice of experimental design and is considered within the purview of the cited prior art. Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Stylli et al. and Photiou et al. because Photiou et al. shown the success of the method for testing compounds for "intracellular biochemical reaction" (e.g. see fig. 1 on pg. 465).

12. Claims 72-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stylli et al. (US Patent 5,985,214) and Photiou et al. (*European Journal of Cancer*, **3/1997**, 33(3), pgs. 463-470) as applied to claims 57, 59-60, 63-71, 76-81, 83, and 85-104 above, and further in view of Walsh, (US Patent 5,990,092).

The instant claim 57 recites a high-throughput method for screening one or more test compounds to identify those that exert an effect on an intracellular biological or chemical process. The method comprises the steps of 1) introducing into each of a plurality of reaction vessels: a plurality of cells, and one or more test compounds whose effect on an intracellular biological or chemical process is to be evaluated; 2) introducing into each of the reaction vessels an antibody characterized in that it associates intracellularly with a biological component whose presence or amount reveals the effect of a given test compound on the biological or chemical process; and 3) assaying for association between the antibody and the component in the reaction vessels. The plurality of reaction vessels comprises at least 96 reaction vessels.

Stylli et al. teaches an automated method and system for identifying chemicals having useful activity such as biological activities of chemicals and collecting informations resulting from such a process (e.g. see Abstract; col. 2, lines 35-41; col. 6, lines 1-24). The method comprise of testing a therapeutic chemical for modulating activity of a target in a cell-based assay (e.g. see col. 38, lines 46-67; col. 39, lines 1-9; col. 43, lines 6-9). The method comprises

dispensing the reagents (compounds) into the addressable sample wells, which contains a predetermined volume of the sample (test cells) (e.g. see col. 6, lines 25-40; col. 8, lines 14-18). Additionally, Stylli et al. disclose the method of dispensing live cell cultures into the sample wells (e.g. see col. 59, lines 20-32). The wells include formats such as 96 wells, 384 wells, or greater (e.g. see col. 15, lines 14-22). Stylli et al. disclose that various different cell-based assay can be employed with its systems wherein the assays include intracellular receptors (e.g. see col. 38, lines 46-47; col. 39, line 60 to col. 40, line 50; col. 42, line 10-15) and also various method of detection of the compound interaction with the target includes fluorescent measurement (e.g. see col. 27, lines 29-35; col. 28, lines 15-17; col. 39, lines 1-67 thru col. 42, lines 1-23). The compounds tested include combinatorial compounds (e.g. see col. 43, lines 21-44).

Furthermore, the features of remaining dependent claims, i.e. volume of the wells or wells format of claims 91-101 are either specifically described by the reference, or constitute obvious variations in parameters which are routinely modified in the art, and which have not been described as critical to the practice of the invention.

Photiou et al. disclose a method for evaluating the in vitro antiproliferative activity (inhibiting cell replication and therefore DNA synthesis) of drugs as single agents and as combinations using human melanoma cell lines G361 and StMl11a (abstract). Photiou et al. disclose an indirect immunofluorescence method in which cells are seeded on glass cover slips placed in 24-well plates, treated with drug(s), fixed, permeated, incubated with rabbit anti-tubulin antibodies, washed, and incubated with goat anti-rabbit antibody conjugated to FITC (secondary ligand) (e.g. see pg. 465, column 1). Photiou et al. discloses the interpretation of the tubulin immunofluorescence data, including the intracellular localization of the primary and

secondary antibodies (e.g. pg. 466, columns 1 and 2). The prevention of tubulin polymerization is a "post-translational event" and an "intracellular biochemical reaction."

The method combination of Stylli et al. and Photiou et al. discloses a high-throughput screening method for test compounds that has an intracellular biological reaction, i.e. cell-base assay, wherein the method steps include introducing into the reaction vessels an antibody that is associated with a biological component and introducing a secondary ligand that binds specifically to the antibody. However, neither of the Stylli et al. or Photiou et al. teaches a cell-base assay wherein 5-bromodeoxyuridine reagent is use as an indicator of intracellular biological reaction.

Walsh et al. discloses an in vitro assay for selecting GATA-6 molecules that modulate vascular smooth muscle proliferation (see example 4 of col. 28). The assay discloses that A7r5 cells (rat) are cultured in media containing the test molecule for up to 72 hours. The cells are harvested at various time points and the proliferative state of the cells is determined by immunohistochemical assays including a BrdU (refers to the claimed reagent of 5-bromodeoxyuridine) assay and a proliferating cell nuclear antigen (PCNA) assay, i.e. an assay for an intracellular antigen (see col. 28, lines 28-44). The assay further discloses that cells are fixed onto a tissue culture dish (reaction vessel), dried, and immunostained using a monoclonal antibody (see col. 28, lines 7-51). The assay discloses that the BrdU assay involves adding BrdU (a reagent known to exert an effect on the process of proliferation) to growth media (containing the cells to be tested) for 24 hours, fixing and permeabilizing the cells, and identifying proliferating cells with a mouse anti-BrdU antibody coupled to FITC (i.e. a second ligand coupled to a fluorescent tag) (col. 27, lines 13-25).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include a cell-base assay wherein 5-bromodeoxyuridine reagent is use as an indicator of intracellular biological reaction as taught by Walsh et al. in the method of Stylli et al. and Photiou et al. One of ordinary skill in the art would have been motivated to include a cell-base assay wherein 5-bromodeoxyuridine reagent is use as an indicator of intracellular biological reaction in the method of Stylli et al. and Photiou et al. since Stylli et al. disclose that any type of cell-base assay can be employed with system of Stylli et al. (e.g. see col. 38, lines 46-47; col. 39, line 60 to col. 40, line 50; col. 42, line 10-15). Thus any type of cell-base assay methodologies can be use in the system of Stylli et al. and the type of cell-base assay use would be a choice of experimental design and is considered within the purview of the cited prior art. Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Stylli et al., Photiou et al., and Walsh et al. because Walsh et al. shown method of cell-base assay wherein 5-bromodeoxyuridine reagent is use as an indicator of intracellular biological reaction in example 4.

Withdrawn Rejection(s)

13. The rejection of claims 58-59, 63, 65, 71-81, 83, 85-104 has been withdrawn in light of applicant's amendments of claim 58 and the withdrawn of claim 58 from consideration as being directed to a non-elected invention.

14. The rejections of claims 57-60, 63-81, 83, and 85-104 under 35 USC 112, second paragraph, as being indefinite have been withdrawn in light of applicant's amendments of claims 57, and 58.

15. The rejections of claims 57-60, 63-81, 83, and 85-104 under 35 USC 112, second paragraph, as being incomplete for omitting essential steps have been withdrawn in light of applicant's amendments of claims 57, and 58 and the withdrawn of claim 58 from consideration as being directed to a non-elected invention.

16. The rejection of claims 57, 69, 71-72, and 88-90 under 35 USC 102(b) as being anticipated by Lam et al. (US Patent 5,510,240) has been withdrawn in light of applicant's arguments regarding that the reference of Lam et al does not teach or suggest the limitation that the assay involve an antibody that associates intracellularly with a biological component, and amendments of claim 57.

17. The rejection of claims 57-60, 63-71, 76-81, 83, and 85-90 under 35 USC 103(a) as being obvious over Photiou et al. (*European Journal of Cancer*, **3/1997**, 33(3), pgs. 463-470) and Lam et al. (US Patent 5,510,240) has been withdrawn in view of applicant's arguments regarding that the reference of Lam et al does not teach or suggest the limitation that the assay involve an antibody that associates intracellularly with a biological component, amendments of claims 57, and 58, and the withdrawn of claim 58 from consideration as being directed to a non-elected invention.

Response to Arguments

18. Applicant's arguments directed to the rejection under 35 USC 103(a) as being unpatentable over Stylli et al. (US Patent 5,985,214) and Photiou et al. (*European Journal of Cancer*, **3/1997**, 33(3), pgs. 463-470) for claims 57, 59-60, 63-71, 76-81, 83, and 85-104 were considered but they are not persuasive for the following reasons.

Applicant contends that the method combination of Stylli et al. and Photiou et al. is not obvious over the presently claimed method because there is no motivation to combine and no reasonable expectation of success in the combination.

Applicant's arguments are not convincing since the method combination of Stylli et al. and Photiou et al. is obvious over the presently claimed method because there is a motivation to combine and reasonable expectation of success in the combination.

First, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine the teaching of Stylli et al. and Photiou et al. is found in the teaching of Stylli et al., i.e. the advantage of providing systems and methods for rapidly processing liquid samples at high throughput rates to identify chemicals with useful activity (see col. 1, lines 50-55). Additionally, Stylli et al. disclose that any type of cell-base assay can be employed with system of Stylli et al. (see col. 38, lines 46-47; col. 39, line 60 to col.

40, line 50; col. 42, line 10-15). Thus, there is a suggestion (motivation) to combine the references of Stylli et al. and Photiou et al.

Second, in response to applicant's argument that there is no reasonable expectation of success to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is a reasonable expectation of success, i.e. obviousness does not require absolute predictability, however, at least some degree of predictability is required. (See MPEP 2143.02). In this case, there is some degree of predictability in the combination of Stylli et al. and Photiou et al. First, Stylli et al. disclose that the prior has shown many known assay have been automated, but the apparatus use is designed for, and dedicated to, a particular type of assay, and Stylli et al. provides the resolution of the problem by designing an apparatus that can be use for any type of assay (see col. 1, lines 14-55; col. 38, lines 46-47; col. 39, line 60 to col. 40, line 50; col. 42, line 10-15). Thus, there is reasonable expectation of success to combine the references of Stylli et al. and Photiou et al. Additionally, applicant supports the argument by citing the reference of the Final Conference Program of LabAutomation'98, i.e. ""*some cell-based assays remain difficult to automate due to the incompatibility of traditional assay platforms with robotics*" (see page 159, first paragraph). The reference of the Final Conference Program of LabAutomation'98 does not show that there is no reasonable expectation of success to combine the references, i.e. Stylli et al. and Photiou et al. Page 159 of the Final Conference Program of LabAutomation'98 (cited by applicant with only half of the sentence) refers the problem of automating a specific type of cell-based assays that is permeable-membrane cell-based assays. However, the second paragraph provides the resolution of such an assay by the

development of an automation-compatible 24-well cell culture membrane insert system. Further, the Final Conference Program of LabAutomation'98 reference teach that high-throughput screening assays in 96-well or 1536-well plates provide advantages in both cost and speed. For example, page 99 recites "*Miniaturization of conventional high-throughput screening assays to the 1 microliter scale in 1536-well plates affords significant advantages in both cost and speed*". Thus, it is unclear how this reference supports applicant assertion that there is no reasonable expectation of success to combine the references Stylli et al. and Photiou et al. Furthermore, the reference of Stylli et al. was filed on 05/16/1997, i.e. before the reference of the Final Conference Program of LabAutomation'98, i.e. 1/17/1998.

Third, applicant's arguments do not rise to the level of factual evidence. See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

Therefore, the method combination of Stylli et al. and Photiou et al. is obvious over the presently claimed method, and the rejection is maintained.

19. Applicant's arguments directed to the rejection under 35 USC 103(a) as being unpatentable over Stylli et al. (US Patent 5,985,214) and Photiou et al. (*European Journal of Cancer*, **3/1997**, 33(3), pgs. 463-470) as applied to claims 57, 59-60, 63-71, 76-81, 83, and 85-104 above, and further in view of Walsh, (US Patent 5,990,092) for claims 72-75 were considered but they are not persuasive for the following reasons.

Applicant contends that the method combination of Stylli et al., Photiou et al., and Walsh

Applicant's arguments are not convincing since is not obvious over the presently claimed method because there is no motivation to combine and no reasonable expectation of success in the combination.

Applicant's arguments are not convincing since the method combination of Stylli et al., Photiou et al., and Walsh is obvious over the presently claimed method because there is a motivation to combine and reasonable expectation of success in the combination.

First, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine the teaching of Stylli et al. and Photiou et al. is found in the teaching of Stylli et al., i.e. the advantage of providing systems and methods for rapidly processing liquid samples at high throughput rates to identify chemicals with useful activity (see col. 1, lines 50-55). Additionally, Stylli et al. disclose that any type of cell-base assay can be employed with system of Stylli et al. (see col. 38, lines 46-47; col. 39, line 60 to col. 40, line 50; col. 42, line 10-15). Thus, there is a suggestion (motivation) to combine the references of Stylli et al., Photiou et al., and Walsh.

Second, in response to applicant's argument that there is no reasonable expectation of success to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed

invention where there is a reasonable expectation of success, i.e. obviousness does not require absolute predictability, however, at least some degree of predictability is required. (See MPEP 2143.02). In this case, there is some degree of predictability in the combination of Stylli et al. and Photiou et al. First, Stylli et al. disclose that the prior has shown many known assay have been automated, but the apparatus use is designed for, and dedicated to, a particular type of assay, and Stylli et al. provides the resolution of the problem by designing an apparatus that can be use for any type of assay (see col. 1, lines 14-55; col. 38, lines 46-47; col. 39, line 60 to col. 40, line 50; col. 42, line 10-15). Thus, there is reasonable expectation of success to combine the references of Stylli et al., Photiou et al., and Walsh. Additionally, applicant supports the argument by citing the reference of the Final Conference Program of LabAutomation'98, i.e. ""*some cell-based assays remain difficult to automate due to the incompatibility of traditional assay platforms with robotics*" (see page 159, first paragraph). The reference of the Final Conference Program of LabAutomation'98 does not shown that there is no reasonable expectation of success to combine the references, i.e. Stylli et al. and Photiou et al. Page 159 of the Final Conference Program of LabAutomation'98 (cited by applicant with only half of the sentence) refers the problem of automating a specific type of cell-based assays that is permeable-membrane cell-based assays. However, the second paragraph provides the resolution of such an assay by the development of an automation-compatible 24-well cell culture membrane insert system. Further, the Final Conference Program of LabAutomation'98 reference teach that high-throughput screening assays in 96-well or 1536-well plates provide advantages in both cost and speed. For example, page 99 recites "*Miniaturization of conventional high-throughput screening assays to the 1 microliter scale in 1536-well plates affords significant advantages in both cost*

and speed". Thus, it is unclear how this reference supports applicant assertion that there is no reasonable expectation of success to combine the references Stylli et al., Photiou et al., and Walsh. Furthermore, the reference of Stylli et al. was filed on 05/16/1997, i.e. before the reference of the Final Conference Program of LabAutomation'98, i.e. 1/17/1998.

Third, applicant's arguments do not rise to the level of factual evidence. See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

Therefore, the method combination of Stylli et al., Photiou et al., and Walsh is obvious over the presently claimed method, and the rejection is maintained.

Conclusion

20. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
May 16, 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER